RECEIVED
CENTRAL FAX CENTER
AUG 07 2006

REMARKS

Please cancel claims 10-11, 13, 15, 18-19, and 24-28 without prejudice. Claims 1-7, 8-9, 12, 14, 16-17, and 20-21 are now pending. The Applicants respectfully request the Examiner to carefully consider the Applicants solicited allowance of the claims now presented in view of amendments to the application and the following remarks.

35 USC §112, Paragraph 1. The Examiner has raised the issue of lack of enablement with regard to claims 10-19.

Claims 10-11, 13, 15, and 18-19 are now cancelled.

The Applicants respectfully point out that the claimed compositions, *per se*, within the scope of claims 12, 14 and 16, are originally characterized as to pharmacological properties in addition to the structural features of the active ingredients. Nevertheless, to expedite the prosecution of this case without prejudice, the Applicants have removed the language that has caused concern.

Claim 17 is now amended to clearly recite a method of treatment of a condition mediated by Peroxisome Proliferator-Activated Receptors (PPAR) comprising administering to a subject in need thereof an effective amount of a compound according to claim 1. PPAR are in fact well-known in the art to mediate type 2 diabetes, dyslipidimia, cardiovascular disease, and syndrome X, for example. Modulation of the biological activity of these receptors is indeed widely-accepted in clinic practice and is well-documented in many preclinical and clinical studies for controlling and treating associated disease conditions including but not limited to human type 2 diabetes and dyslipidemia. The PPARγ agonists Rosiglitazone (AVADIA® from GSK) and Piglitazone (ACTOS® from Takeda), for example, are well-known for treating human type 2 diabetes. PPARα agonists Fenofibrate and Clofibrate, for example, are well-documented for treating human dyslipidemia and hypertention. The Applicants respectfully submit that species representative of the invention are indeed unambiguously exemplified. Figures 1, 2, 3, 4, 5, and 6, for example, illustrate compounds of the present invention to exhibit agonistic activity of PPAR with characteristics of distinct activation profile over PPARγ, PPARγ and PPARα, or PPARα, γ, and δ. Figures 1 and 4, moreover, graphically illustrate comparative activation of PPARα by compounds of the present invention (e.g., Examples 30, 33). Figures 2 and 5, for

example, show comparative activation of PPARγ by compounds of the present invention (Example 31 & 33). Figure 3 and 6, for example, show comparative activation of PPAR heterodimers by compounds of the present invention (Examples 32 and 33). Representative species are further exhibited as efficacious in relevant animal model of *db/db*, a well-established and commonly known transgenic model which mimics late stage pathological changes in human type 2 diabetes (Example 34) as shown in Figure 7.

Representative species are further exhibited as efficacious in relevant animal model of obese rat, a well-established and commonly known model which mimics pathological changes related to non diabetic obesity, insulin-resistance, impaired glucose tolerance, hyperinsulinumia, and dyslipidmia (Examples 35, 36, 37,and 38) as shown in Figures 8 and 9 (*see*, tables 1 and 2).

The Applicants respectfully point out that *some* experimentation by one of ordinary skill to practice the invention as claimed is acceptable under 35 USC §112.1, so long as it is not undue. As a corollary, the Applicants respectfully submit that one of skill in the art can readily practice the invention as claimed in view of the current state of the art -- without undue experimentation, particularly since efficacious compounds that similarly modulate Peroxisome Proliferator-Activated Receptors (PPAR) are well-known in the art.

In summary, one skilled in the art, in view of the state of the art - *and* - the facts of the Applicants' Specification, can easily recognize the disclosure and identification of agonist compounds of the present invention as well as their art-expected use in preventing, controlling, and treating type 2 diabetes, dyslipidimia, cardiovascular disease, and syndrome X, for example.

Accordingly, the Applicants respectfully request the Examiner to withdraw the rejection.

35 USC §112, Paragraph 2, Definite

The Applicants respectfully amend the claims in association with the remarks otherwise presented herewith to address the issues raised by the Examiner. The Applicants respectfully request the Examiner to withdraw the rejection.

35 USC §102. The Examiner alleges that the subject matter of claims 1, 3, 5, and 10-23 is anticipated by Novo Nordisk published U.S. application 20030055076.

The Applicants herein amend the definition of Ar^2 in Formula I to "Ar^2 is a substituted aryl". This amendment separates the claimed subject matter from the genera cited by the Examiner. When Ar^2 is a substituted aryl, the Applicants' disclosed compound CS038 (a 4-fluorophenyl species), for example, compared to an analogous benzene ring compound (CS0381), exhibits clearly distinct agonistic activation against different subtype of Peroxisome Proliferator-Activated Receptors (namely PPARα, γ, and δ). The differences in receptor activation by these compounds directly corresponds to different biological response *in vivo*. The Applicants respectfully request the Examiner to withdraw the rejection.

35 USC §103

The Applicants respectfully submit that the Examiner's rejection is rendered moot in view of the amendments and remarks presented herewith.[1] It is axiomatic that a claimed invention is not obvious solely because it is composed of elements that are all individually found in the prior art. The Applicants respectfully request the Examiner to withdraw the rejection.

* * *

The Applicants respectfully submit that claims 1-7, 8-9, 12, 14, 16-17, and 20-21 are in condition for allowance. Early action toward this end is courteously solicited. The Examiner is kindly encouraged to telephone the undersigned in order to expedite any detail of the prosecution.

---

[1] The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art. In re Kotzab, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references. In re Dance, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998) (there must be some motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the applicant); In re Fine, 837 F.2d 1071, 1075, 5 USPQ2d 1596, 1600 (Fed. Cir. 1988) ("'teachings of references can be combined only if there is some suggestion or incentive to do so.'") (emphasis in original). The need for specificity pervades this authority. See, e.g., In re Kotzab, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000).

The Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 02-4800.

Respectfully submitted,

Patrick H. Higgins
Attorney for the Applicants
Registration No. 39,709

August 7, 2006

Buchanan Ingersoll & Rooney PC
P.O. Box 1404, Alexandria
VA 22313-1404
(609) 987-6811 (voice)